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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,425	11/28/2000	John C. Reed	10412-026	7441

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EXAMINER	
SCHMIDT, MARY M	
ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 02/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,425	REED, JOHN C.	
	Examiner	Art Unit	
	Mary Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14,15,17 and 19-26* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12,14,15,17 and 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This application contains claims 1-7 drawn to an invention nonelected with traverse in Paper No. 5. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

K.T. 2/7

3. Claims ~~8-26~~ 8-12, 14, 15, 17 and 18-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the Official Action mailed 07/03/01.

Applicant's arguments filed 11/05/01 have been fully considered but they are not persuasive.

The claims are drawn to methods of treating a bcl-2 related disorder via administering an effective amount of any anticode oligomer (herein referred to as antisense) wherein said antisense hybridizes to the nucleic acid sequence of SEQ ID NO:19 (a human bcl-2 gene); more specifically, methods of treating cancer such as from the group consisting of non-Hodgkin's lymphoma, prostate cancer, breast cancer, gastro-intestinal cancer or colon cancer; methods of increasing the

sensitivity of tumor cells to chemotherapeutic agents; methods of killing tumor cells; and pharmaceutical compositions comprising said antisense which have implied therapeutic uses.

As argued in the previous action, "although isolated examples are found in the post-art (for treatment effects in whole organisms), they do not correlate to an expectation of those or other antisense oligonucleotides which would hybridize to SEQ ID NO:19 as therapeutic agents since each antisense oligonucleotide functions in a sequence specific manner, having a unique set of enablement issues when used as a therapeutic agent and differs further based on the particular whole organism, the nature of the disease, and routes of administration of the antisense oligonucleotide." (Page 7).

The amended claims are drawn to nucleic acids having 10-40 bases in length for targeting human bcl-2. This amendment to the length of the oligonucleotides does not overcome the unpredictability in the field of antisense design that any nucleotide 10-40 bases would specifically bind and inhibit the target bcl-2 gene for the functions claimed.

Applicants' response is directed to clarification of the test of enablement. Applicant cites several cases to clarify the test for enablement. Applicant argues in the paragraph spanning pages 7 and 8 of the response that subject matter well known to the skilled artisan is preferably omitted from the specification; one skilled in the art is presumed to use the available information in attempting to make and use the claimed invention; and the enablement rules preclude the need for the Applicant to "set forth every minute detail regarding the invention." In response, the factors that are considered unpredictable in the art are precisely the factors which are lacking from the

disclosure. The specific sequence of the oligonucleotides which targets bcl-2, the formulation, dosage, routes of administration and toxicity profiles, are all factors which are not specifically taught in the specification and while are highly unpredictable in the art. Such factors do not correlate from one antisense to another, nor from in vitro to in vivo uses.

Applicant argues in the second paragraph on page 8 that "a disclosure adequately fulfills the enablement requirement if it defines the desired functional relationship, even if some experimentation is required." Applicant further cites the *In re Wands* factors on page 9 and adds that "the test for undue experimentation is not merely quantitative, however, since a considerable amount of experimentation is permissible, so long as it is merely routine." Applicant further states that "while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Customs and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue." In response, Applicants appear to be asserting that since the specification as filed does not teach specific antisense to bcl-2 which have the claimed functions in a whole organism, that it would not be unpredictable in the art for one of skill in the art to design any 10-40 oligomer to bcl-2 for the treatment of any disorder in a human as broadly claimed. In the case of such claims to treatment of a human being with an undeveloped drug, there is always the question of whether such an undefined drug will function to treat any possible disease of that human being. The specific factors considered unpredictable were addressed in the prior Official

Action. Furthermore, the reasons were given as to why general screening of antisense in cells in culture does not correlate to an expectation of success that any such possible antisense will work in a whole organism. The instant specification does not teach how any antisense to bcl-2 can treat any possible disease in a human as broadly claimed. Thus, it is not only the unpredictability in the design and administration of the antisense to a whole organism, but the unpredictability that such administration will be able to treat an undefined set of disorders. In the instant case the specification has neither clearly defined the desired functional relationship such that the specific desired result of the antisense treatment in vivo may be clearly understood. However, if is a specific disease was defined, the unpredictability in the field of antisense further extends to the ability of the antisense to function in the whole organism in the concentration and target specificity needed to achieve the desired effect. In a complex whole organism such as a human, the lack of understanding of all the physiological pathways and cause and effect of administration of a novel drug candidate precludes the expectation that any potential drug candidate will function in a specific pattern that solves the problem disease. In light of this complexity of the whole organism, and the arguments above, there would be an undue amount of experimentation required to make and use the invention claimed.

On page 10 of the response, Applicant further argues that "it is well-settled that the inclusion of undisclosed species within a broad genus does not necessarily render a claim unduly broad.... Inoperative species within a broad claim are clearly permissible.... a broad claim can be enabled by the disclosure of a single embodiment." Applicant further argues on page 11 that the

specification teaches screening methods for operable embodiments of bcl-2 antisense. Applicant further points out that the instant SEQ ID NO:17 is now known in the art to be useful as a treatment against non-Hodgkin's lymphoma. In response, the instant disclosure does not provide the support that one of skill in the art would have been able to make and use any bcl-2 antisense in a whole organism since no guidance was provided that would have allowed the skilled artisan at the time the invention was made to use any such antisense in a whole organism for treatment of any disease as claimed. Although the post-art teaches the success of specific antisense for specific disorders, these results were not available at the time the instant disclosure the pertinent art as a whole did not provide the guidance later taught for the specific antisense sequence, formulation, route of administration and treatment effects taught in the post-art.

For the reasons stated above, the arguments do not overcome a *prima facie* case of lack of enablement for the claimed invention to any antisense to bcl-2 for treatment of any human disease.

4. The prior art does not teach nor fairly suggest design and administration of antisense to bcl-2 for treatment of whole organisms as instantly claimed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
February 5, 2002

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
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